Docket No. 1073.060
U.S. Serial No. 09/595,096

Amendments to the Specification:

Please replace the second paragraph on page 1 (the first paragraph of the Background section) with the following amended paragraph.

"Prediction of small molecule binding modes to macromolecules of known three-dimensional structure is a problem of paramount importance in rational drug design (the "docking" problem)... Protein binding sites exhibit highly selective recognition of small organic molecules, in that evolution has equipped them with a complex three-dimensional "lock" into which only specific "keys" will fit. This has been exploited by medicinal chemists in the design of molecules to selectively augment or retard biochemical pathways and so exhibit a clinical effect. X-ray crystallography has revealed the structure of a significant number of these binding sites. It would be advantageous in attempting the computer-aided design of therapeutic molecules to be able to predict and to explain the binding mode of novel chemical entities (the "docking" problem) when the active site geometry is known." (Jones *et al., J. Mol. Bio.* 267, pg. 727 (1997)) With the advent of combinatorial chemistry and the resulting ability to synthesize large collections of compounds for a broad range of targets, it has become apparent that the capability to effectively prioritize screening efforts is crucial to the rapid identification of the appropriate region of chemical space for a given target. Since it has been generally observed that hits obtained against a given target are clustered in a finite region of chemical space, there is reason to believe that given the right computational tools it is possible to prioritize screening efforts such that only libraries containing active compounds are interrogated. Effective prioritization tools would allow scientists to both obtain leads in a cost effective and efficient manner and to test virtual libraries against novel targets prior to active synthesis and bioanalysis, thereby, reducing synthesis costs. With the expected flood of new targets becoming available in the coming decade, it will be critical to focus screening efforts on target appropriate regions of chemical space.

Please replace the last paragraph on page 20 with the following amended paragraph.

To test the docking procedure, the GOLD test set was used (see Jones, G., et al., "Development and Validation of a Generic Algorithm for Flexible Docking," Journal of Molecular Biology, 1997, Vol. 267, p. 727-748, which is hereby incorporated herein by reference in its entirety). For the test set, "protein-ligand complexes were selected from the Protein Data Bank (Bernstein, *J. Mol. Biol.*, 112, 535-542 (1977)). These complexes were selected on the basis of

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pharmacological interest and whether the ligands involved were 'drug-like'." (Jones, *J. Mol. Biol.*, 267, 728 (1997) Any covalently bound ligand or any ligand bound to a metal ion was removed because it cannot, at present, be modeled by the scoring function described herein. In addition, any "surface sugars" were removed as they are not typical of the problems encountered. This left a total of 103 cases (sec Table 1 below). No further individual processing of the test cases was performed. (Note that the "Protein Data Bank" (PDB) is a database where target molecule structures are placed. The "PDB Code" is a four letter code that allows a given structure to be found and extracted from the PDB.)

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